

Web Table 1: DEHP General Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Animal Number/ Sex	Dose ^a	Body Weight	Organ/Body Weight	Histopathology	Hematology	Chemistry	Other
B6C3F ₁ Mice Hazelton 1992 (1)	Subchronic study – 4 weeks. 6-week-old mice were fed diets with DEHP at 1,000, 5,000, 10,000, or 25,000 ppm and were then killed and necropsied. Hematology and serum chemistry (glucose, BUN, creatinine, liver enzymes, electrolytes) were evaluated at week 5.	10	0						
		10	245(M)/ 270(F)	NE	NE	NE	NE	NE	NOAEL
		10	1,209(M)/ 1,427(F)	↓(M)	↑Li ↓Ki (M)	Li effects Ki effects (M)	↓Hb (M) ↓Hct(M)	NE	LOAEL
		10	2,579(M)/ 2,897(F)	↓(M)	↑Li ↓Te	Li and Ki effects	Hb, Hct	NE	
		10	6,992(M)/ 7,899(F)	↓	↑Li ↑Ki (F) ↓Te	Li, Ki, Th, Te, and Ov effects	↓Hb, Hct ↓RBC (M)	*	Death in 4/10 M and 3/10 F. Clinical signs.

^aDoses measured in mg/kg bw/day.

*Statistical analysis not possible due to small sample sizes. Few surviving animals at higher doses.

NA=Not Analyzed

NE=No Effects

M=Male

F=Female

↓=Statistically Significant Decrease

↑= Statistically Significant Increase

RBC=Red Blood Cell

Th=Thymus

Ov=Ovary

Te=Testes

Li=Liver

Ki=Kidney

Hb=Hemoglobin

Hct=Hematocrit

Web Table 2: DEHP General Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Animal Number/ Sex	Dose ^a	Body Weight	Testes	Liver	Other
Sprague-Dawley Rats Poon et al. 1997 (2)	Subchronic study—13 weeks. Male and female rats (~4–6 weeks old*) were fed diets with 0, 5, 50, 500, or 5,000 ppm DEHP for 13 weeks, then sacrificed and necropsied. Analyses were conducted for hematology, clinical chemistry, and histopathology. Peroxisome proliferation was examined microscopically.	10	0				
		10	0.4(M)/0.4(F)	NE	NE	NE	
		10	3.7(M)/4.2(F)	NE	NE	↓ASAT(M)	NOAEL
		10	38(M)/42(F)	NE	Sertoli cell vacuolation.	↓ALAT(F) ↓ASAT	LOAEL
		10	375(M)/419(F)	NE	Sertoli cell vacuolation and seminiferous tubule atrophy. ↓Sperm count. ↓Te/body weight ratio.	↑Peroxisomes (by electron microscopy). Liver cell enlargement. Mild focal necrosis in 1 male and 2 females. ↓ASAT(M) ↑APD, AH ↓Ch(F) ↑Alb(M) ↑Li/body weight ratio.	↓Colloid density and follicle size in thyroid. ↑Ki/body weight ratio. ↓RBC, Hb(M), PC, MCV. ↑Ca (M), PO ₄ , K(M), protein (F).

^aDoses measured in mg/kg bw/day.

*Based on Charles Rivers growth chart for males weighing 105–130 g and females weighing 93–111 g.

NA=Not Analyzed

NE=No Effects

↑= Statistically Significant Increase

↓=Statistically Significant Decrease

MCV=Mean Corpuscular Volume

ASAT=Aspartate Aminotransferase

M=Male

F=Female

Li=Liver

Ki=Kidney

PO₄=Inorganic Phosphate

Te=Testes

ALAT=Alanine Aminotransferase

APD=Aminopyrine-N-demethylase

AH=Aniline Hydroxylase

Ca=Calcium

K=Potassium

Hb=Hemoglobin

RBC=Red Blood Cells

Alb=Albumin

Ch=Cholesterol

PC=Platelet Count

Web Table 3: DEHP General Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Animal Number/ Sex	Dose ^a	Body Weight	Organ/ Body Weight	Histopathology	Hematology	Chemistry	Other
F344 Rats	Subchronic study – 13 weeks.	10							
Hazelton 1992 (3)	8-week-old rats were fed diets with DEHP at 0, 1,000, 4,000, 12,500, or 25,000 ppm and then were killed and necropsied. Analyses were conducted for hematology, clinical chemistry, urinalysis, organ weight, and histopathology.	10	63(M)/73(F)	NE	↑Li(M)	NE	NE	NE	LOAEL
		10	261(M)/302(F)	NE	↑Ki(M), ↑Li	Slight Li (M) effects.	↓RBC(M).	↑ (M): BUN, TP, Al. ↓Glo.	
		10	850(M)/918(F)	↓(F)	↑Ki, ↑Li	Ki and Li effects.	↓RBC(M), Hct(M), and Hb(M).	↑ (M): Glu, TP. ↑BUN, Al ↓Glo.	Clinical signs.
		10	1,724(M)/1,858(F)	↓*	↓Ut, Te ↑BrS, Ki, ↑Li	Pi(M), Ad, St(M), Ki, and Li effects. Te atrophy and aspermia.	↓RBC(M). ↓Hb, Hct.	↑Glu, BUN, TP(M), Alb. ↓Glo.	Clinical signs. ↑Urine blood (M). ↓Urine protein (M). ↓Urine pH (F).

^a Doses measured in mg/kg bw/day.

*Decreased food consumption.

NA=Not Analyzed

NE=No Effects

M=Male

F=Female

↓=Statistically Significant Decrease

↑= Statistically Significant Increase

NS=Non-significant

Th=Thymus

Ov=Ovary

Te=Testes

Li=Liver

Ki=Kidney

Glu=Glucose

BUN=Blood Urea Nitrogen

TP=Total Protein

Alb=Albumin

Glo=Globulin

RBC=Red Blood Cells

Pi=Pituitary

Ad=Adrenals

St=Stomach

Ut=Uterus

BrS=Brain stem

Hb=Hemoglobin

Hct=Hematocrit

Web Table 4: DEHP General Toxicity, Marmosets

Species, Strain, and Source	Experimental Regimen	Animal Number/ Sex	Dose^a	Body Weight	Organ/ Body Weight	Histopathology	Hematology	Chemistry	Other
Marmoset	Subchronic study – 13 weeks. Pubescent male and female marmosets were gavaged with DEHP in corn oil for 13 weeks and then sacrificed and necropsied.	4	0						
Kurata et al. 1998		4	100	NE	NE	NE	NA	NE	No effects on testicular zinc
(4)		4	500	NE	NE	NE	NA	NE	
		4	2,500	↓(M)	NE	↑ Peroxisomal volume (M). No effects in testes or pancreas.	NA	NE	NOAEL

^a Doses measured in mg/kg bw/day

NA=Not Analyzed

NE=No Effects

M=Male

F=Female

↓=Statistically Significant Decrease

↑= Statistically Significant Increase

Web Table 5: DEHP General Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Animal Number/ Sex	Dose ^a	Body Weight	Organ Weight	Histopathology	Hematology	Chemistry	Other
Wistar Rat Klimisch et al. 1992 (5)	Subchronic Study – 4 weeks. 9-week-old rats inhaled DEHP mists (0, 0.01, 0.05, and 1.0 mg/l) 6 hours/day, 5days/week, for 28 days. 10 rats/sex/group were killed and necropsied after exposure and peroxisome proliferation was evaluated in 2 rats/sex/group. 15 male rats/group were mated to untreated females for 10 days at 2 and 6 weeks following exposure and fertility was evaluated. 5 rats/sex/group were killed and necropsied 8 weeks following exposure.	5–15	0						
		5–15	2.3(M)/3.6(F)	NE	NE	NE	NE	NA	NE
		5–15	11(M)/18(F)	NE	NE	NE	NE		NOAEL
		5–15	230(M)/360(F)	NE	↑ Lu (reversible, M).	Alveolar septum thickening and foam-cell proliferation (reversible).	↑ Alb ↑ PO ₄ (M) (reversible).		NE on male fertility as determined by mating success, fertility index, and implantation loss.
					↑ Li (reversible).	NE, including peroxisome proliferation. NE on male sex organs.			

^a Doses measured in mg/kg bw/day.

NA=Not Analyzed

NE=No Effects

M=Male

F=Female

↓=Statistically Significant Decrease

↑= Statistically Significant Increase

Alb=Albumin

PO₄=Inorganic Phosphate

Lu=Lung

Li=Liver

Web Table 6: 2-EHA General Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Animal Number/ Sex	Dose ^a	Body Weight	Organ/ Body Weight	Histopathology	Hematology	Chemistry	Other
F344 Rat Juberg et al. 1998 (6)	Subchronic study – 13 weeks.6-week-old male and female rats were fed diets with 0, 0.1, 0.5, or 1.5% 2-EHA for 13 weeks and then sacrificed and necropsied.	10	0						
		10	61(M)/ 71(F)	NE	NE	NE	NE	↑Ch(M).	
		10	303(M)/ 360(F)	NE	↑Te, Li, Ki(F).	Hepatocyte hypertrophy (M).	↓MCH, MCV.	↑Ch(M).	
		10	917(M)/ 1,068(F)	↓	↑Te, Li, Ki.	Hepatocyte hypertrophy.	↓MCH, MCV.	↑Ch(M) ↑Alb(M).	

^a Doses measured in mg/kg bw/day.

*Organ to body weight ratio.

NA=Not Analyzed

NE=No Effects

M=Male

F=Female

↓=Statistically Significant Decrease

↑= Statistically Significant Increase

Ki=Kidney

Li=Liver

St=Stomach

Ov=Ovaries

Te=Testes

Ch=Cholesterol

Alb=Albumin

MCH=Mean Corpuscular Hemoglobin

MCV= Mean Corpuscular Volume

Web Table 7: 2-EHA General Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Animal Number/ Sex	Dose^a	Body Weight	Organ/ Body Weights	Histopathology	Hematology	Chemistry	Other
B6C3F ₁ Mice Juberg et al. 1998 (6)	Subchronic study – 13 weeks. 6-week-old male and female mice were fed diets with 0, 0.1, 0.5, or 1.5% 2-EHA for 13 weeks then sacrificed and necropsied.	10	0						
		10	180(M)/ 205 (F)	NE	NE	NE	NE	NE	
		10	885(M)/ 1,038(F)	NE	↑Li, Ki(F)	Hepatocyte hypertrophy (M).	NE	↑Ch. ↓Tg and Bi (F).	
		10	2,728(M)/ 3,139(F)	↓	↑Te, Li, Ki(F)	Hepatocyte hypertrophy and lesions, kidney lesions, and stomach lesions(M).	NE	↑Ch(M). ↓Tg, Bi. ↑ALAT(M).	

^a Doses measured in mg/kg bw/day.

NA=Not Analyzed

NE=No Effects

M=Male

F=Female

↓=Statistically Significant Decrease

↑= Statistically Significant Increase

Ki=Kidney

Li=Liver

St=Stomach

Ov=Ovaries

Te=Testes

Ch=Cholesterol

Tg=Triglycerides

Bi=Bilirubin

ALAT=Alanine Amino Transferase

Web Table 8: 2-EH General Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Animal Number/ Sex	Dose ^a	Body Weight	Organ/ Body Weight	Histopathology	Hematology	Chemistry	Other
F344 Rat Astill et al. 1996 (7)	Subchronic study – 13 weeks. Male and female rats (42–43 days-old) were gavaged with 2-EH in chromophore 5 days/ week, for 13 weeks then sacrificed and necropsied.	10	0						
		10	25	NE	NE	NE	NE	NE	
		10	250	NE	↑Ki, Li. ↑St(F), Ov	NE	NE	↓ALAT (F).	
		10	500	↓	↑Ki, Li, St, Te (63%).	Stomach and liver lesions, adrenal hyperplasia.	↑Re	↓ALAT and Ch (F). ↓Pr and Alb (M).	↑ Peroxisomal enzymes.

^a Doses measured in mg/kg bw/day.

NA=Not Analyzed

NE=No Effects

M=Male

F=Female

↓=Statistically Significant Decrease

↑= Statistically Significant Increase

Ki=Kidney

Li=Liver

St=Stomach

Ov=Ovaries

Te=Testes

Re=Reticulocytes

ALAT=Alanine Aminotransferase

Ch=Cholesterol

Pr=Protein

Alb=Albumin

Web Table 9: 2-EH General Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Animal Number/ Sex	Dose ^a	Body Weight	Organ/Body Weight	Histopathology	Hematology	Chemistry	Other
B6C3F ₁ Mice Astill et al. 1996 (7)	Male and female mice (49–61 days-old) were gavaged with 2-EH in chremophore 5 days/ week, for 13 weeks then sacrificed and necropsied.	10	0						
		10	25	NE	NE	NE	NE	NE	
		10	250	NE	↑ Li, ↑ St(M).	NE	NE	NE	
		10	500	NE	↑ Li, ↑ St(M).	Stomach lesions.	NE	NE	No effect on peroxisomal enzymes.

^a Doses measured in mg/kg bw/day.

M=Male

NE=No Effects

↓=Statistically significant decrease

↑= Statistically significant increase

Ki=Kidney

St=Stomach

Li=Liver

Web Table 10: DEHP Developmental Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Number*	Dose ^a	Maternal Effects	Fetal Effects
CD-1 Mice Tyl et al. 1988; Tyl et al. 1984 (8, 9)	Prenatal developmental toxicity study. DEHP administered in feed on gd 0–17, at 0, 0.025, 0.05, 0.10, or 0.15%. Sacrificed on gd 17. Dams weighed on gd 0, 4, 8, 12, 16, and 17. Maternal liver and uteri weighed, and corpora lutea counted at sacrifice. All fetuses examined for gross external, visceral, and skeletal malformations.	30	0		
		26	44	NOAEL	NOAEL
		26	91	↑Lethargy and rough coat.	↑Fetuses/litter with malformations (14 vs 2.5%).
		24	191	↓Weight gain (not corrected). ↑Liver to body weight ratio. ↑Lethargy and rough coat. ↓Piloerection.	↑Resorptions/litter (52 vs 16%) and litters with resorptions (96 vs 60%). ↑Non-live implants/litter (55 vs 16%). ↓Live litter size (n = 8.1 vs 11.0). ↓Fetal body weight (8%; female). ↑Fetuses/litter with malformations (47 vs 2.5%).**
		25	293	↓Weight gain (not corrected). ↑Liver to body weight ratio. ↑Lethargy and rough coat.	↑Resorptions/litter (84 vs 16%) and litters with resorptions (100 vs 60%). ↑Non-live implants/litter (85 vs 16%). ↓Live litter size (n = 5.6 vs 11.0). ↓Fetal body weight (16%). ↑Fetuses/litter with malformations (92 vs 2.5%).**

^a Doses measured in mg/kg bw/day.

*Number of pregnant dams at sacrifice.

**External, visceral, and skeletal.

↑=Statistically Significant Increase

↓=Statistically Significant Decrease

n=number

gd=gestation day

Web Table 11: DEHP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number*	Dose**	Maternal Effects	Fetal Effects
Fischer-344 Rats Tyl et al., 1988; Tyl et al. 1984 (9, 10)	Prenatal developmental toxicity study. DEHP administered in feed on gd 0–20 at 0, 0.5, 1.0, 1.5, or 2.0%. Sacrificed on gd 20. Dams weighed at gd 0, 4, 8, 12, and 20. Maternal liver and uteri weighed and corpora lutea counted at sacrifice. Fetuses examined for gross external, visceral, and skeletal malformations.	24	0		
		23	357	NOAEL ↑ Relative liver weight. ↓ Food consumption. ↑ Water intake.	NOAEL
		22	666	Piloerection and rough coat. ↑ Relative liver weight. ↓ Gestational weight gain. ↓ Corrected weight gain. ↓ Food consumption. ↑ Water intake.	↓ Fetal weight (6%).
		24	856	Piloerection and rough coat. ↑ Relative liver weight. ↓ Gestational weight gain. ↓ Corrected weight gain. ↓ Food consumption. ↑ Water intake.	↓ Fetal weight (15%).
		25	1,055	Piloerection and rough coat. ↑ Relative liver weight. ↓ Gestational weight gain. ↓ Corrected weight gain. ↓ Food consumption.	↑ Resorptions (54 vs 4%) and affected implants (58 vs 5%). ↓ Fetal weight (25%). ^a ↑ Skeletal variations Trend of fetal malformations (1.27, 0, 1.92, 3.13, and 2.87%).

*Number of pregnant dams at sacrifice.

** Doses measured in mg/kg bw/day.

^aNot statistically significant.

↓=Statistically Significant Decrease

↑=Statistically Significant Increase

n=number

gd=gestation day

Web Table 12: DEHP Developmental Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Number ^a	Dose*	Maternal Effects	Fetal Effects
CD-1 Mice	Prenatal developmental toxicity study. DEHP administered by gavage on gd 6–15. Sacrificed on gd 17. Dams weighed on gd 0, 2, 6, 9, 12, 15, and 17. Maternal liver and placenta were weighed, corpora lutea were counted, and implantation sites examined. All fetuses were weighed and examined for gross external malformations. Visceral and skeletal malformations were examined in half the fetuses.	30	0		
Huntingdon		14	40	NE	NOAEL
1996		14	200	NOAEL	↑ External and visceral malformations/ variations. ^b
(11)		13	1,000	↓ Weight gain (gd 6–17). ↑ Liver to body weight ratio.	↓ Pup survival. ↑ Resorptions (n=5.6/11 litters vs 0.6/30 litters) and post implantation losses (41 vs 4.4%). ↓ Fetal weight (7%). ↑ Skeletal variations. ^b ↑ Skeletal, external, and visceral malformations. ^b

* Doses measured in mg/kg bw/day.

^a Number of pregnant dams at sacrifice.

^b Fetal malformations/variations were not statistically analyzed.

↑=Statistically Significant Increase

↓=Statistically Significant Decrease

NE=No Effects

n=number

gd=gestation day

Web Table 14: DEHP Developmental Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Number*	Dose**	Maternal Effects	Fetal Effects
CD-1 Mice	Pre- and postnatal developmental toxicity study. DEHP administered in diet on gd 0–17 at 0, 0.01, 0.025, or 0.05%. Dams weighed every 4 days and allowed to litter. Pups were weighed and examined at birth and then evaluated for development and sexual maturation. F ₁ pups were mated within parental dose groups (F _{2a} litter) and between high dose and control groups (F _{2b} litter). F ₂ pups were examined on pnd 1 and 4 and then sacrificed. Sex organs of control and high dose F ₁ rats were weighed and examined histologically.	26	0		
Price et al. 1988		26	19	NE	NE
(12)		26	48	NE	NOAEL
		25	95	NOAEL	<p>↑ Prenatal mortality/litter in F₁ pups (26 vs 9.0%).</p> <p>↓Live F₁ pups/litter (n=8.5 vs 10.9).</p> <p>↓Live F_{2a} pups/litter (n=9 vs 11).</p> <p>↓F₁ Pup survival on pnd 4 (85 vs 96%).</p> <p>No effects on F₁ developmental landmarks, including vaginal opening and testes descent, or sex organ weight and histology at any dose.</p> <p>No effects on growth and viability of F₂ litters at any dose.</p>

*Number of dams with a live litter on pnd 1.

** Doses measured in mg/kg bw/day.

NE=No Effect ↑=Statistically Significant Increase

↓=Statistically Significant Decrease n=Number gd=gestation day

Web Table 15: DEHP Reproductive Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Number ^a	Dose (mg/kg bw/day)	Effects
CD-1 Swiss Mice Reel et al., 1984; Lamb et al., 1987 (13, 14)	Fertility assessment through continuous breeding study. DEHP administered to breeding pairs in feed (0, 0.01, 0.1, and 0.3%) for 98 days. Body weight, clinical observations, and food intake recorded. Number of conceptions, number and size of litters, and deaths counted and pup weight measured. Crossover mating conducted on the 0 and 425 mg/kg bw dose group. After mating period, breeding pairs sacrificed and necropsied. Specific organs weighed and histologically examined for the 0 and 425 mg/kg bw/kg dose groups.	40^b 20 19 18	0 14^b 141 425	NOAEL ↓ Fertility in treated pairs (4/19 fertile). ↓ Number of litters (34%). ↓ Live pups/litter (51%). Complete infertility was observed in F ₀ pairs. ↓ Male (4/20) and female (0/16) fertility in crossover study. ↓ Testicular (60%), epididymal (20%), and prostate (12%) weight. ↓ Motile sperm (60%) and sperm concentration (79%). ↑ Abnormal sperm (665%). ↓ Testosterone (52%); ↑ FSH (42%) and LH (28%). ↓ Female reproductive tract weight (16%). ↑ Relative liver weight.

^aNumber of breeding pairs.

^bNumbers in bold text represent NOAELs.

↑=Statistically Significant Increase

↓=Statistically Significant Decrease

FSH=Follicle Stimulating Hormone

LH=Luteinizing Hormone

Web Table 16: DEHP Reproductive Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number*	Dose (mg/kg bw/day)	Effects
Wistar Rats Schilling et al. 1999 (15)	Fertility assessment through a 2-generation reproductive toxicity study. DEHP administered in feed (0, 1,000, 3,000, or 9,000 ppm) for 70 days prior to mating until the end of the lactation period. Rats were mated for ≤ 2 weeks. Food intake and body weights were measured weekly. Reproductive data evaluated included mating, fertility, gestation, and live birth index. Pups were sexed, weighed, and evaluated for anogenital distance, survival, and sexual development. At the end of lactation, F ₀ rats were sacrificed and necropsied and liver and sex organs were weighed. Testes were examined histologically in F ₀ males and 1 F ₁ rat/litter. All but 1 male and female F ₁ rat/litter were examined and sacrificed.	10/10	0	
		10/10	110	↓ F ₁ pup survival on pnd 1–4.
		10/10	339	↑Liver to body weight ratio in F ₀ (15–23%). ↓ F ₁ pup survival to pnd 21. Loss of spermatocytes in 2/10 F ₁ pups.
		10/9	1,060	↓Gestational weight gain in F ₀ dams. ↑Weight loss during lactation in F ₀ dams. ↓Food intake during gestation and lactation in F ₀ dams. ↑Liver to body weight ratio in F ₀ (38–39%). ↓Absolute ovary weight in F ₀ (25%). No effects on F ₀ testicular histology. ↑Postimplantation loss in F ₀ dams. ↓ F ₁ litter size and liveborn pups (34%). ↓ F ₁ pup survival on pnd 1–4. ↓ F ₁ pup weight gain. ↑Areolas/nipples in male F ₁ pups (84 vs 0%, transient). ↑Time for vaginal opening (by 3 days) and preputial separation in F ₁ pups (by 4 days). Lose of spermatocytes in 7/9 F ₁ pups. Testicular lesions in F ₁ .
	Selected F ₁ rats continued to receive the same DEHP concentrations as parents and at sexual maturity were mated within dose groups for ≤ 2 weeks. The parameters evaluated were the same as those in F ₀ rats. F ₁ rats and their litters were sacrificed on pnd 2. Sex organs of F ₁ males were weighed and examined histologically.	10/10	0	
		10/10	110	NE
		8/8	339	NE
		6/5	1,060	Death in 3/9 F ₁ males and 2/9 F ₁ females. ↓Gestational weight gain in F ₁ dams. ↑Liver to body weight ratio in F ₁ males (33%). ↓Testes to body weight ratio in F ₁ males (22%). ↓Absolute epididymis weight in F ₁ males (20%). ↓F ₂ litter size (34%) and liveborn pups. ↓Anogenital distance in male F ₂ pups (13%).

NE=No Effect *Number of pairs/pairs producing a litter ↑=Statistically Significant Increase ↓=Statistically Significant Decrease pnd=postnatal day

Web Table 17: DEHP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number ^a	Dose*	Maternal Effects	Fetal Effects
Long-Evans Rat Arcadi et al. 1998 (16)	Pre- and postnatal developmental toxicity. DEHP administered in drinking water (32.5 and 325 µL/L) to dams throughout gestation and lactation. Liver, kidney, and testes were weighed and examined histologically in 1 pup/8 litters/group on pnd 21, 28, 35, 42, and 56. Neurobehavioral function was tested by having female pups walk on a beam to avoid negative stimuli on pnd 30.	12	0	No effects on body weight gain or appearance	↑Liver to body weight ratio. ↓Testes to body weight ratio (12%). ↓Absolute kidney weight (reversible). Reversible histological changes in liver and kidney. Histological changes in testes.
		12	3.0-3.5		
		12	30-35		

* Doses measured in mg/kg bw/day.

^aNumber of treated dams.

↑=Statistically Significant Increase

↓=Statistically Significant Decrease

pnd=postnatal day

Web Table 18: DEHP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Numbers ^a	Dose*	Maternal effects	Developmental effects
Wistar Rats Hellwig et al. 1997 (17)	Prenatal developmental toxicity study. DEHP administered in oil by gavage on gd 6–15. Dams weighed on gd 0, 6, 10, 15, and 20 and sacrificed on gd 20. Maternal uteri were weighed, corpora lutea were counted and implantation sites examined. Fetuses were weighed and examined for gross external malformations. Half the fetuses were examined for visceral malformations and the other half for skeletal malformations.	10 9 10 9	0 40 200 1,000	 NE NOAEL ↑Liver and kidney to body weight ratio. ↓Uterine weight. ↓Body weight gain.	 NOAEL ↑Postimplantation loss (40 vs 10%). ↑Resorptions (40 vs 9.8%). ↓Fetal weights (18%). ↑Fetus/litter with malformations (63 vs 2%), variations (80 vs 25%), and retardations (57 vs 39%). ^b ↑Litters with malformations (100 vs 10%). ^b

* Doses measured in mg/kg bw/day.

^aNumber of pregnant dams at sacrifice.

^bExternal, soft tissue, and skeletal.

NE=No Effects

↑=Statistically Significant Increase

↓=Statistically Significant Decrease

Web Table 19: DEHP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Numbers	Dose**	Maternal effects	Developmental effects
Fischer-344 Rat Narotsky and Kavlock 1995 (18)	Prenatal developmental toxicity screen. DEHP administered in oil by gavage on gd 6–19. Dams were weighed on gd 6, 8, 10, 13, 16, and 20. Dams were allowed to litter. Pups were counted, weighed and examined on pnd 1 and 6. Implantation sites and resorptions were examined in dams.	13 ^a	0		
		10	1,125	Delayed parturition. Vaginal bleeding. Weight loss (<10%). Piloerection.	100% prenatal pup loss. Eye and vascular defects.*
		9	1,500	Delayed parturition. Vaginal bleeding. Weight loss (<10%). Piloerection.	~98% prenatal pup loss. 1 live born pup dead by pnd 6. Cleft palate and renal agenesis (1 pup).*
Fischer-344 Rat Narotsky et al. 1995 (19)	The developmental toxicity screen was repeated with lower doses with administration of DEHP on gd 6–15.	12 ^b	0		
		11	333	NE	NE
		10	500	NOAEL	NOAEL
		11	750	Delayed parturition.	Eye defects (in 2.8% pups).
		12	1,125	Delayed parturition.	Eye defects (in 4.3% pups).

** Doses measured in mg/kg bw/day.

^aNumber of pregnant dams.

^bNumber of treated dams.

*A few dead pups were available for examination but the number available was not stated.

NE=No Effects

pnd=postnatal day

Web Table 20: DEHP Developmental Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Treatment day	Number*	Dose**	Maternal effects ^a	Fetal effects ^a
ddY-Slc Mice Yagi et al., 1980; Nakamura et al. 1979; Tomita et al., 1982 (20-22)	Prenatal developmental toxicity study. DEHP administered by gavage. Not a full factorial dose experiment. Sacrificed on gd 18. Maternal corpora lutea counted. Fetuses examined for gross external, and skeletal malformations.		4-31	0		
		gd 6	6	2,465		↓ Fetal weight
		gd 7	22	49.3	No effects at 4 lowest doses.	No effects at two lowest doses.
			11	49.3		
			6-10	986		
			5	2,465		High incidence of death and abnormalities.
			4	4,930	↓Weight gain	
		gd 8	5	9,860	↓Weight gain	High incidence of death and abnormalities. ↓ Fetal weight
			6	7,395		
			8	9,860		
		gd 9	3	7,395	↓Weight gain	Lower incidence of death and abnormalities. ↓ Fetal weight.
			5	9,860		
			5	29,580		
		gd 10	7	9,860	↓Weight gain	Lower incidence of death and abnormalities.
			7	29,580		

* Number of pregnant females at sacrifice.

** Doses measured in mg/kg bw/day.

^a Effects described apply to all doses given on the specified gestational day, unless otherwise indicated.

↑=Statistically Significant Increase

gd=gestation day

↓=Statistically Significant Decrease

Web Table 21: DEHP Developmental Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Numbers*	Dose**	Maternal effects	Developmental effects
ICR-JCL Mice Shiota et al., 1980; 1982 (23, 24)	Prenatal developmental toxicity study. DEHP administered in feed on gd 0–18 at 0, 0.05, 0.1, 0.2, 0.4, and 1.0%. Dams weighed on gd 0–18. Sacrificed on gd 18. Maternal corpora lutea counted. Fetuses examined for skeletal malformations or soft tissue morphology.	8	0		
		8	70	NE	LOAEL Delayed ossification.
		9	190	NOAEL	↑ Prenatal mortality (31 vs 5%).
		7	400	↓ Body weight on gd 18.	↑ Prenatal mortality (68–83 vs 5%). ↑ Fetuses with malformations (26–41 vs 0%). ↓ Fetal weight (14–38%). Delayed ossification.
		7	830	↓ Body weight on gd 18.	Complete prenatal mortality.
		12	2,200	↓ Body weight on gd 18.	Complete prenatal mortality.

*Number of pregnant females at sacrifice.

** Doses measured in mg/kg bw/day.

↑=Statistically Significant Increase

NE=No Effect

↓=Statistically Significant Decrease

Web Table 22: DEHP Developmental Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Numbers**	Dose*	Maternal effects	Developmental effects
ICR Mice Shiota & Mima, 1985 (25)	Four prenatal developmental toxicity studies. DEHP administered by gavage on gd 7–9. Sacrificed on gd 18. Fetuses examined for gross external, visceral, and skeletal malformations. Lethality and abortion were the only maternal effects reported	11	0		
		9	250	NE	Fetuses with malformations (4.3 vs 0.3%). ^b
		10	500	NE	Fetuses with malformations (26 vs 0.3%).
		10	1,000^a	NOAEL	↑Fetuses with malformations (37 vs 0.3%). ↑ Number of resorptions (59 vs 9%). ↓ Fetal weight (F: 9%; M:20%).
		11	2,000	Low incidence of lethality.	↑Fetuses with malformations (83 vs 0.3%). ↑ Number of resorptions (93 vs 9%). ↓ Fetal weight (F: 17%; M: 28%).
	DEHP administered IP on gd 7–9. Sacrificed on gd 18. Fetuses examined for gross external, visceral, and skeletal malformations.	9	0		
		3	500	NE	NE
		4	1,000	NE	NE
		9	2,000	NE	NE
		8	4,000^a	NOAEL	NOAEL
		3	8,000	↑ Number of abortions (2/3 dams).	↑ Prenatal mortality. ↑ Number of resorptions (80 vs 7%).

* Doses measured in mg/kg bw/day.

**Number of pregnant females at sacrifice.

^aNumbers in bold indicate NOAELs.

^bDose dependent.

↑=Statistically Significant Increase

↓=Statistically Significant Decrease

NE=No Effect

gd=gestation day

IP=intraperitoneally

Web Table 23: DEHP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Animal Number**	Dose*	Maternal effects	Fetal effects
Wistar Rats Ritter et al., 1987 (26)	Prenatal developmental toxicity study. DEHP administered by gavage on gd 12. Sacrificed on gd 20. Fetuses were weighed and examined for viability, gross external, visceral, and skeletal malformations.	7	0	Not reported.	
		7	4,882		↑ Fetuses with malformations (4.5 vs 0%). ^a ↑ Prenatal mortality and fetal resorptions (10.9 vs 9.6%). ^a
		7	9,764		↑ Fetuses with malformations (21 vs 0%). ^a ↑ Prenatal mortality and fetal resorptions (15.5 vs 9.6%). ^a

* Doses measured in mg/kg bw/day.

** Number of pregnant dams at sacrifice.

↑=Statistically Significant Increase

^aStatistical significance unknown.

↓=Statistically Significant Decrease

gd=gestation day

Web Table 24: DEHP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Numbers ^a	Dose*	Maternal effects	Developmental effects
<i>Rattus norvegicus</i> (Albino) Rats Srivastava et al., 1989 (27)	Prenatal developmental toxicity study. DEHP administered by gavage on gd 6–15. Sacrificed on gd 20. Fetal livers examined for enzyme levels. Fetuses were counted and weighed. Fetuses were examined for viability, gross external, visceral, and skeletal malformations.	21 21	0 1,000	 ↓ Gestational weight gain.	 ↑ Relative liver weight (23%). ↓ Activity of mitochondrial liver enzymes (22–44%). ↓ Fetal weight (24%).

* Doses measured in mg/kg bw/day.

^aNumber of pregnant dams at sacrifice.

↑=Statistically Significant Increase

↓=Statistically Significant Decrease

gd=gestation day

Web Table 25: DEHP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Numbers**	Dose*	Maternal effects	Developmental effects
Sprague-Dawley Rats Lewandowski et al., 1980 (28)	Prenatal developmental toxicity study. DEHP plasma extracts administered intravenously on gd 6–15. Dam weights and gross physical changes recorded daily. Sacrificed on gd 20. Fetuses were weighed counted, and examined for gross external, visceral, and skeletal malformations.	25	0.0		
		25	1.3 ^a	NE	NE
		25	4.7 ^a	NE	NE
		25	1.4 ^b	NE	NE
		25	5.3 ^b	NE	NE
Sprague-Dawley Rats Singh et al., 1972 (29)	Prenatal developmental toxicity study. DEHP administered by intraperitoneal injection on gd 5, 10, and 15. Sacrificed on gd 20. Maternal corpora lutea were counted. Fetuses weighed and examined for viability, gross external and skeletal malformations..	5	0		
		5	4,930	Not reported.	↑ Fetal resorptions (8.2 vs 0%). ↓ Fetal weight (27%).
		5	9,860		↑ Fetal resorptions (27 vs 0%). ↑ Fetuses with malformations (22 vs 0%). ↓ Fetal weight (28%).

* Doses measured in mg/kg bw/day.

**Number of pregnant dams at sacrifice.

↑=Statistically Significant Increase

^a DEHP extracted from strips of PL-130 plastic.

↓=Statistically Significant Decrease

^b DEHP extracted from strips of PL-146 plastic.

NE=No Effects

Web Table 26: DEHP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Numbers ^a	Treatment Day	Dose ^b	Maternal effects	Developmental effects
Sprague-Dawley Rats Peters and Cook 1973 (30)	Prenatal developmental toxicity study. Rats were injected IP with saline or DEHP on specified gestation days. Dams were allowed to litter. Implantation sites were examined in dams that died or delivered dead pups.	10	gd 1	0	***	↓Live pups (9.4 vs 10–11.2). ↓Pups weaned (7.2 vs 10).
		5		1,972		
		4	gd 3	1,972	***	Implantations in 4/5dams. ↓Live pups (8.3 vs 10–11.2). ↓Pups weaned (6.7 vs 10)
		4	gd 6	1,972	2 dams killed.	Implantations in 4/5dams. ↓Live pups (8.5 vs 10–11.2). ↓Pups weaned (8.5 vs 10).
		5	gd 9	1,972	5 dams killed.	
		3	gd 3, 6	1,972	***	Implantations in 3/5dams. ↓Live pups (9.0 vs 10–11.2). ↓Pups weaned (9.0 vs 10).
		5	gd 6, 9	1,972	1 dam died. Bleeding during delivery.	NE
		4	gd 3, 6, 9	1,972 ^{**}	1–3 dams died. Bleeding during delivery.	Implantations in 2–4/5dams. ↓Live pups (4.0–5.0 vs 10–11.2). ↓Pups weaned (4.0–5.0 vs 10).
	Surviving female offspring were mated and allowed to litter	5 *		3,944 All dose groups	 1 dam died. Bleeding during delivery. Not reported.	 Implantations in 1/5 dams. No effects on litter size.

^aDams with implants. ^b Doses measured in mg/kg bw/day.*Numbers mated not indicated.

^{**}Includes data from 2 experiments.

^{**}No maternal toxicity reported for these dose groups

↑=Statistically Significant Increase

↓=Statistically Significant Decrease

NE=No Effects

Web Table 27: DEHP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Numbers ^a	Dose ^b	Maternal effects	Offspring effects
Wistar Rats	Pre- and postnatal developmental toxicity study. DEHP administered by inhalation (0, 0.01, 0.05, or 0.3 mg/L) for 6 hours/day on gd 6–15. Dams weighed at gd 3, 6, 9, 12, 15, & 20. 20 females/group were killed on gd 20 and examined for resorption sites. Fetuses were examined for external, skeletal and visceral malformations. 5 Females/group allowed to litter. Dams weighed on days pnd 7 and 21. Physical development (non-sexual) of pups assessed. Pups sacrificed and examined on pnd 21.	18 (5)	0		
Merkle et al., 1988		19 (5)	2.8	NE	NE
(31)		17 (5)	14^c	NE	NOAEL
		16 (5)	84	↓ Body weight (pnd 21).	↓ Live fetuses/dam (n=10.6 vs 12). ^d ↑ % Litters with skeletal retardations ^e (56 vs 17%). No differences were observed for postnatal survival or non-sexual development at any dose level.

^aNumber of litters evaluated on gestation day 20 (number of litters delivered).

^bDoses (in mg/kg bw/day) calculated by IEHR.

^cNumbers in bold text represent NOAELs.

^dSince not dose-dependent, not considered treatment related.

^eMay not be treatment related due to high incidence of this type of skeletal retardation in Wistar rats and as well as the control groups.

↑=Statistically Significant Increase
pnd=Postnatal day

↓=Statistically Significant Decrease

NE=No Effect

n=Number

gd=Gestation day

Web Table 28: DEHP Developmental Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Numbers ^a	Dose*	Maternal effects	Fetal effects
F ₄ C57BL/6N X Sv/129, wild type mice Peters et al. 1997 (32)	Prenatal developmental toxicity. DEHP administered by gavage on gd 8–9. Dams weighed on gd 0, 8, 9,10 and 18. Sacrificed on gd 10 or 18. Maternal liver was weighed, and liver mRNA and zinc analysis conducted on gd 10. Implantation sites examined on gd 10 and 18. Fetuses were examined for neural tube defects and zinc levels on gd 10 and weighed and observed for gross external malformations on gd 18.	10–12 10	0 1,000	↓Body weight gain (gd 18). ↑Liver/body weight ratio (gd 10). ↑Liver metallothionein and zinc level (gd 10). ↑CYP4A1 mRNA transcription (gd 10).	↑Resorptions (72 vs 15%; gd 18). ↓Live fetuses (34 vs 88% on gd 10; 28 vs 84% on gd 18). ↓Fetal weight (9%). ↓Crown-rump length (26%; gd 10). ↑Neural tube defects (78 vs 8% on gd 10). ↑Fetuses with external abnormalities (40 vs 3% on gd 18). ↓Fetal zinc level (gd 10).

* Doses measured in mg/kg bw/day.

^aNumber of litters examined on gd 10 and 18.

↑=Statistically Significant Increase
↓=Statistically Significant Decrease

gd=gestation day

Web Table 29: MEHP Developmental Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Number ^a	Dose*	Maternal effects	Fetal effects
CD-1 Swiss Mice Price et al., 1991 (33)	Prenatal developmental toxicity study. MEHP administered in feed gd 0–17 at 0, 0.017, 0.035, 0.07, or 0.14%. Dams weighed gd 0–17. Sacrificed on gd 17. Fetuses counted, weighed, and sexed. Fetuses examined for gross external, visceral, and skeletal malformations.	26	0		
		28	35	NE	LOAEL
		27	73	NE	↑ Litters with resorptions (63 vs 28%).
		27	134	NOAEL ↑ Relative liver weight.	↑ Litters with resorptions (74 vs 28%). ↑ Fetuses with malformations (25 vs 3%). ↓ Fetal weight (7%).
		27	269	↓ Adjusted weight gain. Relative liver weight.	↑ Litters with resorptions (93 vs 28%). ↑ Fetuses with malformations (42 vs 3%). ↓ Fetal weight (6%).

*Doses measured in mg/kg bw/day.

^a Number of pregnant females at sacrifice.

↑=Statistically Significant Increase

↓=Statistically Significant Decrease

gd=gestation day

NE=No Effect

Web Table 30: MEHP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Numbers ^a	Dose*	Maternal effects	Fetal effects
Wistar Rats Ruddick et Al., 1981 (34)	Prenatal developmental study. MEHP Administered by gavage on gd 6–15. Dams weighed on gd 0 and 18. Dams sacrificed on gd 22. Maternal deciduomas counted. Pups counted and litters weighed. Pups examined for visceral and skeletal malformations.	13	0		
		15	50	NOAEL	NE
		10	100	↓ Gestational weight gain.	NE
		13	200	↓ Gestational weight gain. ^b	NE
		9	225	↑ Maternal lethality. ↓ Gestational weight gain. ^b	NOAEL
		8	450	↑ Maternal lethality. ↓ Gestational weight gain. ^b	↓ Number of dams with live litters (n = 6/11 vs 13/15). ↓ Litter weight (8%).
		0	900	Complete maternal lethality.	

*Doses measured in mg/kg bw/day.

^aNumber of pregnant females at sacrifice.

↑=Statistically Significant Increase

↓=Statistically Significant Decrease

NE=No Effect

^bNot statistically significant.

n=Number

gd=gestation day

Web Table 31: MEHP Developmental Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Number ^a	Dose [*]	Maternal effects	Fetal effects
ICR Mice Shiota & Mima, 1985 (25)	Prenatal developmental toxicity study. MEHP administered by gavage on gd 7–9. Sacrificed on gd 18. Fetuses examined for gross external, visceral, and skeletal malformations.	11	0		
		13	50	NOAEL	NE
		12	100	↑ Number of abortions.	NE
		9	200	↑ Maternal lethality. ↑ Number of abortions.	NE
		0	400	Complete maternal lethality.	
	MEHP administered intraperitoneally on gd 7–9. Sacrificed on gd 18. Fetuses examined for gross external, visceral, and skeletal malformations. Dams and fetuses sacrificed on gd 18.	9	0		
		14	50	NOAEL	NE
		12	100	↑ Maternal lethality.	NE
		0	200	Complete maternal lethality.	

^{*}Doses measured in mg/kg bw/day.

^aNumber of pregnant females at sacrifice.

↑=Statistically Significant Increase

↓=Statistically Significant Decrease

NE=No Effect

Web Table 32: MEHP Developmental Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Animal Number	Treatment Day	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects
DdY-Slc Mice Yagi et al. 1980 Tomita 1982 (20, 22)	Prenatal developmental toxicity study. MEHP administered by gavage on gd 7, 8, or 9. Not a full factorial dose experiment. Sacrificed on gd 18. Maternal corpora lutea counted. Fetuses examined for gross external and skeletal malformations.	9		0		
		6	<u>gd 7</u>	104	*	↓Fetal weight. ↑Fetal death.** ↑Abnormalities.**
		4		1,040		↓Fetal weight. ↑Fetal death.**
		8	<u>gd 8</u>	104	*	↑Fetal death.** ↑Abnormalities.**
		5		520		↓Fetal weight. ↑Fetal death.** ↑Abnormalities.**
		2		1,040		↓Fetal weight. ↑Fetal death.** ↑Abnormalities.**
		3	<u>gd 9</u>	1,040	*	↓Fetal weight. ↑Fetal death.** ↑Abnormalities.**

*Decreases in maternal weight gain were observed, but it is not clear at which doses and exposure days.

**Statistical significance not indicated.

↑=Statistically Significant Increase

gd=gestation day

↓=Statistically Significant Decrease

Web Table 33: MEHP Developmental Toxicity, Rabbits

Species, Strain, and Source	Experimental Regimen	Number^a	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects
New Zealand White Rabbits Thomas et al. 1979 (35)	Prenatal developmental toxicity study. MEHP administered intravenously on gd 6–18. Dams weighed daily and sacrificed on gd 30. Maternal corpora lutea and implantation sites examined and organs were weighed and examined histologically. Fetuses were weighed and examined for gross external malformations. Half the fetuses were examined for visceral malformations and the other half for skeletal malformations.	22 (15)	0	1/22 Died	
		11 (5)	1.1	NE	NE
		11 (8)	5.7	2/11 Died.* Convulsions prior to death.	NE
		11 (7)	11.4	4/11 Died.* Convulsions prior to death. Paralysis in 2/11 does. Abortion in 1 doe. No changes in organ weights at any dose.	10 Resorptions in 1litter. No increases in fetal malformations at any dose.

^aNumber of dams treated (Number of dams pregnant at sacrifice).

*Authors stated that deaths appeared to be unrelated to treatment.

NE=No Effect

gd=gestation day

Web Table 34: 2-EH Developmental Toxicity, Mice

Species, Strain, and Source	Experimental Regimen	Number*	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects
CD-1 Mice Tyl et al., 1991 (36, 37)	Prenatal developmental toxicity study. 2-EH administered by microcapsule in feed (0, 0.009, 0.03, or 0.09%) on gd 0–17. Dams weighed on gd 0, 3, 6, 9, 12, 15, and 17. Sacrificed on gd 17. Maternal liver, and uterus weighed, and corpora lutea counted. Fetuses counted, weighed, and sexed. Fetuses examined for gross external, visceral, and skeletal malformations.	27	0		
		27	17	NE	NE
		27	59	NE	NE
		26	191	↑Food consumption (gd 0–3).	NE

*Number of dams pregnant at sacrifice

↑=Statistically Significant Increase

NE=No Effect

gd=gestation day

Web Table 35: 2-EH Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number*	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects ^a
Wistar Rats Ritter et al. 1987 (26)	Prenatal developmental toxicity study. 2-EH administered by gavage on gd 12 (6.25 and 12.5 mmol/kg). Sacrificed on gd 20. Implantation sites examined. Fetuses weighed and observed for viability and external, visceral, and skeletal malformations.	7	0	Not reported	
		7	814		↓Fetal weight (5%). ↑Malformations (2 vs 0%). ↑Resorptions (10.1 vs 9.6%).
		7	1,629		↓Fetal weight (15%). ↑Malformations (22 vs 0%).

*Number of litters evaluated.

^aStatistical significance of effects is not clear.

↑=Statistically Significant Increase

gd=gestation day

↓=Statistically Significant Decrease

Web Table 36: 2-EH Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number ^a	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects
Wistar Rat Hellwig et al. 1997 (38)	Prenatal developmental toxicity study. 2-EH administered in water with 0.005% Cremophor EL by gavage on gd 6–15. Dams were weighed daily and sacrificed on gd 20. Maternal uteri were weighed, corpora lutea were counted and implantation sites examined. Fetuses were weighed and examined for gross external malformations. Half the fetuses were examined for visceral malformations and the other half for skeletal malformations.	19 (270)	0		
		10 (130)	130	NE	NE
		9 (127)	650	“Slight maternal toxicity visible.”	↓Fetal weight (9.5%).
		2 (28)	1,300	Death in 6/10 dams. Decreased body weight gain and food intake. Discolored liver, pulmonary edema, and clinical signs of toxicity.	↑Resorptions/dam and postimplantation loss. ↓Fetal weight (25%). ↑Fetuses with malformations, variations , and retardations. ^b

^aTotal number of litters (fetuses) evaluated.

^bDilated renal pelves, anal defects, and skeletal effects.

↑=Statistically Significant Increase

NE=No Effect

n=number

↓=Statistically Significant Decrease

Web Table 37: 2-EH Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number*	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects
Sprague-Dawley Rat	Prenatal developmental toxicity study.	15	0		
Nelson et al. 1989 (39)	Dams breathed 2-EH vapors (0 or 850 mg/m ³) for 7 hours/day on gd 1–19. Dams were weighed weekly and sacrificed on gd 20. Corpora lutea were counted and implantation sites examined. Fetuses were weighed, sexed and examined for gross external malformations. Half the fetuses were examined for visceral malformations and the other half for skeletal malformations.	15	262 ^a	↓Food intake (~10–15%).	↑Delayed ossification. ^b

*Number of treated rats.

^aCalculated with average dam body weight (312.5 g) and EPA (1988) assumptions for daily inhalation rate (0.330 m³/day) ^bEffect was not statistically significant.

↑=Statistically Significant Increase

gd=gestation day

↓=Statistically Significant Decrease

Web Table 38: 2-EH Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number*	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects
Fischer 344 Rats Tyl, 1989 (40)	Prenatal developmental toxicity study. 2-EH administered by occluded cutaneous application for 6 hours/day on gd 6–15. Dams weighed on gd 0, 6, 12, 15, 18, and 21. Sacrificed on gd 21. Maternal liver, and intact uterus weighed, and corpora lutea counted. Fetuses counted, weighed, and sexed. Fetuses examined for gross external, visceral, and skeletal malformations.	18	0		
		19	252	NE	NE
		23	840	Cellular exfoliation and erythema.	NE
		20	2,520	Cellular exfoliation and erythema. ↓ Gestational weight gain.	NE

*Number of dams pregnant at sacrifice.

NE=No Effect

↓=Statistically Significant Decrease

gd=gestation day

Web Table 39: 2-EHA Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number*	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects
Fischer 344 Rats Tyl, 1988 (41)	Prenatal developmental toxicity study. 2-EHA administered by gavage on gd 6–15. Dams weighed on gd 0, 6, 12, 15, 18, and 21. Sacrificed on gd 21. Maternal liver and intact uterus weighed, and corpora lutea counted. Fetuses examined for gross external, visceral, and skeletal malformations.	25	0		
		25	100^b	NE	NOAEL
		25	250^b	NOAEL.	↑ Skeletal variations ^a .
		25	500	↑ Clinical signs of toxicity. ^c ↑ Relative liver weight.	↑ Skeletal variations. ↓ Weight (8%).

*Number of pregnant females at sacrifice.

^aNot statistically significant.

^bNumbers in bold text represent NOAELs.

^cClinical signs included hypoactivity, ataxia, audible respiration, ocular discharge, and periocular encrustation.

↑=Statistically Significant Increase

NE=No Effect

↓=Statistically Significant Decrease

gd=gestation day

Web Table 40: 2-EHA Developmental Toxicity, Rabbits

Species, Strain, and Source	Experimental Regimen	Number*	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects
New Zealand White Rabbits Tyl et al. 1988 (42)	Prenatal developmental toxicity study. 2-EHA administered by gavage on gd 6–18. Dam weight measured on gd 0, 6, 9, 12, 15, 18, & 21. Sacrificed on gd 21. Maternal liver and uterus weighed, and corpora lutea counted. Fetuses were counted, weighed, and sexed. Fetuses were examined for gross external, visceral, and skeletal malformations.	15	0		
		15	25^a	NOAEL	NE
		11	125	1 Maternal fatality. ^b 1 Aborted litter. ^b	NE
		13	250^a	1 Maternal fatality. ^b ↓ Weight gain (gd 18–29). ↓ Food consumption (gd 18–29).	NOAEL

* Number of pregnant females at sacrifice.

^aNumbers in bold text represent NOAELs.

^bAlthough not statistically significant, the authors believe these effects to be treatment related.

↓=Statistically Significant Decrease
gd=gestation day

NE=No Effect

Web Table 41: 2-EHA Developmental Toxicity, Rats

Species, Strain, and Strain	Experimental Regimen	Number*	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects
Wistar Rats	Prenatal developmental toxicity study. 2-EHA administered by gavage on gd 12 (6.25 and 12.5 mmol/kg). Sacrificed on gd 20. Implantation sites examined. Fetuses weighed and observed for viability and external, visceral, and skeletal malformations.	7	0	Not reported	↓Fetal weight (2.4%). ↑Malformations (0.8 vs 0%). ↑Resorptions (12.9 vs 9.6%). ↓Fetal weight (29%). ↑Malformations (68 vs 0%).
Ritter et al. 1987 (26)		7	902		
		7	1,803		

*Number of litters evaluated.

^aStatistical significance of effects is not clear.

↑=Statistically Significant Increase
 ↓=Statistically Significant Decrease

gd=gestation day

Web Table 42: 2-EHA Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Animal Number	Dose (mg/kg bw)	Maternal Effects	Fetal Effects*
Sprague-Dawley Rats Scott et al. 1998 (43)	Prenatal developmental toxicity study. 2-EHA administered by gavage on gd 12. Sacrificed on gd 20. Implantation sites examined. Fetuses were observed, sexed, and weighed. 2/3 were examined for visceral malformations and 1/3 for skeletal malformations.	10	0	Not reported	↑Resorptions (14 vs 6%). ↓Fetal weight (28%). ↑Malformations (37 vs 1%). ↑Resorptions (60 vs 6%). ↓Fetal weight (47%). ↑Malformations (100 vs 1%).
		9	1,803		
		7	2,253		

*Statistical significance not reported.

↑=Statistically Significant Increase
 ↓=Statistically Significant Decrease

gd=gestation day

Web Table 43: 2-EHA Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number*	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects
Han:Wistar Rats Pennanen et al., 1992 (44)	Prenatal developmental toxicity study. 2-EHA administered in drinking water on gd 6–19. Dams sacrificed on gd 20. Maternal liver and uterus weighed, and corpora lutea counted. Fetuses examined for gross external, visceral, and skeletal malformations.	21	0	NE	↑ Fetuses with variations.
		21	100		
		20	300^a	NOAEL	↑ Fetuses with malformations. ↓ Mean fetal/litter weight (6%; F). ↓ Placental weight. ↑ Fetuses with variations.
		20	600		
				↓ Corrected weight gain. ↑ Water consumption	↑ Fetuses with malformations. ↓ Mean fetal/litter weight (8%; F). ↓ Placental weight. ↑ Fetuses with variations.

*Number of pregnant females at sacrifice.

^aNumbers in bold text represent NOAELs.

↑=Statistically Significant Increase

↓=Statistically Significant Decrease

NE=No Effect

F=Female

Web Table 44: 2-EHA Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number *	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects
Han:Wistar Rats Pennanen et al., 1993 (45)	Postnatal developmental toxicity study. 2-EHA administered in drinking water prior to mating (males 10 weeks; females 2 weeks) and females on gd 0–20. Maternal liver and uterus were weighed, and corpora lutea counted. Pups were counted and examined for gross external malformations. Pups were weighed on pnd 0, 4, 7, 14, and Pups were evaluated daily for developmental parameters. Sacrificed on pnd 21.	23	0		
		21	100^a	NE	NOAEL
		24	300^a	NOAEL	↑ Incidence of kinky tail (24 vs 5%). Delay in developmental parameters. ↓ Litter size (n= 9.2 vs 10.9).
		23	600	↓ Water consumption.	↑ Incidence of kinky tail (26 vs 5%). Delay in developmental parameters.

*Number of pregnant females at sacrifice.

^aNumbers in bold text represent NOAELs.

↑=Statistically Significant Increase

NE=No Effect

gd=gestation day

↓=Statistically Significant Decrease

n=number

pnd=postnatal day

Web Table 45: 2-EHA Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number*	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects
Sprague-Dawley Rats Bui et al. 1998 (46)	Prenatal developmental toxicity study. 2-EHA administered by gavage on gd 8–15 to dams fed adequate zinc diets. Sacrificed on gd 16 or 19. Resorptions, fetal weight, and external and skeletal malformations evaluated on both sacrifice days.	7–10	0		
		7–10	483	↓ Corrected body weight (gd 16 and 19).	↑Resorptions (23 vs 5%) in gd 19 group only. ↓Fetal weight (9%) and crown-rump length (9%) in gd 19 group only. ↑Brain/skull (14 vs 0%) and tail (26 vs 2%) malformations/litter in gd 16 group. ↑Tail malformations/litter (7.9 vs 0%) in gd 19 group.**

*Number of litters evaluated on sacrifice day 19 and 16, respectively.

** Not statistically significant.

↑=Statistically Significant Increase

gd=gestation day

↓=Statistically Significant Decrease

Web Table 46: Phthalic Acid Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number ^a	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects
Wistar Rat Ema et al. 1997 (47)	Prenatal developmental toxicity study. Phthalic acid administered in diet (0, 1.25, 2.5, or 5.0%) on gd 7–16. Dams were weighed daily and sacrificed on gd 20. Corpora lutea and implantation sites were examined and fetal survival was evaluated. Fetuses were weighed and examined for gross external malformations. 1/3 of the fetuses were examined for visceral malformations and 2/3 for skeletal malformations.	11	0		
		11	1.021	NOAEL	NE
		11	1,763	↓ Weight gain and food intake.	NOAEL
		11	2,981	↓ Weight gain and food intake.	↓Male fetus weight. ↓Ossification. No effects on fetal survival or malformations.

^aNumber of pregnant dams at sacrifice.

↓=Statistically Significant Decrease

NE=No Effect

gd=gestation day

Web Table 47: DEHP Reproductive Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number ^a	Dose (mg/kg bw/day)	Effects
Fischer-344 Rats Agarwal et al., 1986 (48)	Male reproductive toxicity study. DEHP administered to males in feed (0, 320, 1,250, 5,000, or 20,000 ppm) for 60 days prior to mating. Body weight and food intake recorded weekly. Housed with 2 virgin females for 5 days. Number of conceptions, number and size of litter, deaths and pup weight measured. After mating, selected males sacrificed and necropsied. Selected organs weighed and histologically examined in 8 males/group. Other males allowed to recover for up to 65 days.	24	0	
		24	18	NE
		24	69	NE
		24	284	↑ Relative liver weight. ↓ Body weight gain (transient).
		24	1,156	Testicular atrophy observed histologically. ↓ Epididymal sperm motility (48%) and density (37%). ↑ Abnormal sperm observed (550%). ↓ Mean litter size (15%). ↓ Relative testis and epididymal weights and absolute prostate weight. ↑ Relative liver weight. ↓ Body weight gain. ↓ Testicular zinc. ↑ Serum FSH.

^aNumber of treated males.

↑=Statistically Significant Increase
↓=Statistically Significant Decrease

NE=No Effect
FSH=Follicle Stimulating Hormone

Web Table 48: DEHP Developmental Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Number ^a	Dose (mg/kg bw/day)	Maternal Effects	Fetal Effects
Sprague Dawley Rat Gray et al. 1999 (49)	Pre and postnatal developmental toxicity study. DEHP administered in oil by gavage from gd 14 to lactation day 3. Male pups were examined for sexual maturation. At 5 months of age, male offspring were killed and necropsied. Organ weights were measured and a histological examination was conducted on reproductive organs	9 8	0 750	Not reported	<p>↓Anogenital distance (2.45 vs 3.70mm).</p> <p>↓Pup weight on gd 2 (17%).</p> <p>↑Percentage of areolas (88 vs 0%) and numbers of areolas/nipples (n=8 vs 0).</p> <p>↑% Hypospadias (67 vs 0%), vaginal pouches (45 vs 0%), prostate agenesis (14%), and testicular and epididymal atrophy or agenesis (90 vs 0%).</p> <p>↓Seminal vesicle, prostate, epididymis, testes, and penis weight.</p>

^aNumber of litters evaluated.

↑=Statistically Significant Increase
↓=Statistically Significant Decrease

n=Number
gd=gestation day

Web Table 49: 2-EHA Reproductive Toxicity, Rats

Species, Strain, and Source	Experimental Regimen	Animal Number	Dose (mg/kg bw/day)	Effects
Wistar Rats Pennanen et al., 1993 (45)	Reproductive toxicity study. 2-EHA administered in drinking water to males for 10 weeks prior to breeding, to females 2 weeks prior to breeding, to both sexes during breeding, and to females during gestation and lactation. Food and water intake recorded. Males and non-pregnant females were sacrificed and necropsied following breeding. Specific male organs weighed and histologically examined. Pregnant females allowed to litter. Number of conceptions, number and size of litters, number of deaths, counted. Pups weighed on pnd 0, 4, 7, 14, and 21. Physical development of pups evaluated. Pups examined for gross malformations	23 ^a	0	
		23	100	↓ Motile sperm (35 vs 22%).
		24	300	↑ Incidence of kinky tail (24.5 vs. 4.9%) and lethargy (26.7 vs 0%). Delayed physical development of pups.
		24	600	↑ Incidence of kinky tail (25.6 vs. 4.9%). ↑ Epididymal weight (17%). ↓ Motile sperm (27 vs 35%). ↓ Gestational weight gain (21%). ↓ Female water consumption. ↓ Litter size (15%). Delayed physical development of pups. Delayed fertilization. No effects on testicular histology.

^aNumber of breeding pairs.

↑=Statistically Significant Increase

↓=Statistically Significant Decrease

Web Table 50: DEHP General Toxicity, Monkeys

Species, Strain, and Source	Experimental Regimen	Animal Number/ Sex	Dose (mg/kg bw/day)	Body Weight/Organ Weight	Histopathology	Hematology/ Chemistry	Other
Cynomolgus monkey Pugh et al. 2000 (50)	Sub-acute study – 2 weeks. 2-year-old males were gavage treated with DEHP in 0.5% methylcellulose for 2 weeks and then sacrificed and necropsied	4 4	0 500	 NE	 Liver lesions in 1 animal. No testicular lesions.	 NE	 No peroxisomal proliferation. No effects on gap junctional intracellular communication.

NA=Not Analyzed

NE=No Effects

M=Male

F=Female

↓=Statistically Significant Decrease

↑= Statistically Significant Increase

Web Table 51: DEHP General Toxicity, Marmosets

Species, Strain, and Source	Experimental Regimen	Animal Number/ Sex	Dose (mg/kg bw/day)	Body Weight	Organ Weight	Histopathology	Hematology	Chemistry	Other
Marmoset	Subacute study – 2 weeks. 12–18-month-old male and female marmosets were gavaged treated with DEHP in corn oil for 2 weeks and then sacrificed and necropsied.	5	0						
Rhodes et al. 1986 (51)		5	2,000	↓	NE	NE reported for testes or other organs.	NA	↑ Catalase.	No increase in peroxisomal proliferation.

NA=Not Analyzed

NE=No Effects

M=Male

F=Female

↓=Statistically Significant Decrease

↑= Statistically Significant Increase

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